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Case Report:
Cornelia De-Lange Syndrome

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Abstract:

Cornelia de-Lange syndrome is characterized by distinctive facial dysmorphism, primordial short stature, hirsutism, and upper limb reduction defects that range from subtle phalangeal abnormalities to oligodactyly. Craniofacial features include synophrys, arched eyebrows, long eyelashes, small widely spaced teeth and microcephaly. IQ ranges from between 30 and 102 with an average of 53. Many individuals demonstrate autistic and self-destructive tendencies. It is an autosomal dominant disorder caused by specific gene mutations and occurrence is one in 10,000 to 50,000 children. This is a case report of a 2 1/2-year-old female child with Cornelia de-Lange syndrome phenotype.

Keywords: Cornelia de-Lange syndrome (CdLS), synophrys, cleft palate.

Introduction:

Cornelia de-Lange syndrome (CdLS) was first described as a distinct syndrome in 1933, by Dr.Cornelia de-Lange, a Dutch Pediatrician, after whom the disorder has been named, though the first ever documented case was reported in1916 by Dr. Brachmann.[1] A gene responsible for CdLS–NIPBL on chromosome 5–was discovered in 2004 by researchers at Children's Hospital of Philadelphia. In 2006, a second gene–SMC1A on the X chromosome–was found by Italian scientists. A third gene discovery was announced in 2007.[2] The gene SMC3 is on chromosome 10 and was also discovered by the research team in Philadelphia. The latter two genes seem to correlate with a milder form of the syndrome. Majority of cases are due to spontaneous mutations, but this syndrome also has an autosomal dominant inheritancepattern. The types of mutations seen in CdLS rarely include large deletions and 50% have detectable point mutations (frame shift, splice site, nonsense and missense).[3]

Most of the signs and symptoms of CdLS may be recognized at birth or even prenatally by ultrasound imaging. The incidence is 1 case per 10,000 to 50,000 births.[1] No difference based on race and sex has been reported. Most children could not live more than 2 years and the main cause of death was pneumonia along with cardiac, respiratory and gastrointestinal abnormalities.[2]

Currently diagnosis is made on the basis of clinical observations.[4] A thorough medical evaluation including a history and physical examination, family history, laboratory tests, X-rays and chromosome analysis is usually conducted before a diagnosis is made. DNA testing is helpful for confirmation of a clinical diagnosis, but the sensitivity is only 50% for mutations in NIPBL.

There is the potential for CdLS to be caused by other genes which have yet to be identified.

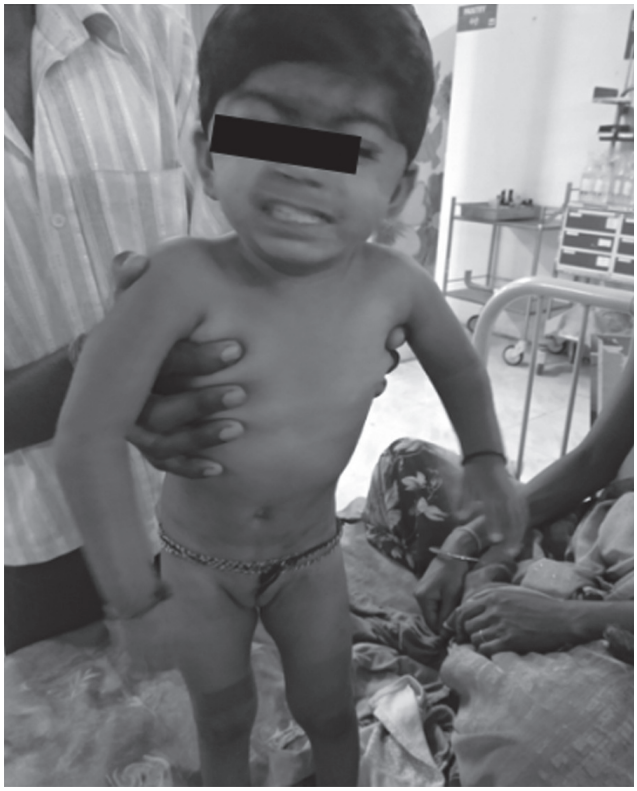
CdLS has been characterized by retardation in growth, distinctive facial dysmorphism, primordial short stature, psychomotor delay, behavioural problems, hirsutism and upper limb reduction defects that range from subtle phalangeal abnormalities to oligodactyly.[5]

Reports of craniofacial features of CdLS include micro brachycephaly, synophrys, arched eyebrows, long eyelashes, depressed nasal bridge, anteverted nares, long philtrum, thin upper lip, high arched palate, late eruption of small widely spaced teeth, micrognathia, spurs in the anterior angle of mandible and prominent symphysis.[6] The estimated prevalence of CHD in CdLS varies between 14% and 70% in previously studied patient cohorts of between 10 and 310 individuals, with several studies reporting a prevalence near 25%[7]. A variety of defects have been described, with ventricular and atrial septal defects being the most common; complex heart defects such as tetralogy of Fallot and single ventricle anomalies have also been described.

In this paper, we report a case of CdLS phenotype, along with radiographic and other investigations.

Case Report

A 2 1/2 -year-old female patient with CdLS, who demonstrated the classic facial features of the syndrome, reported with a chief complaint of cleft palate and came for further management. Birth history showed that the patient was born by normal vaginal delivery,birth weight was 2 kg and did not cry immediately after birth for which patient was admitted in NICU for a duration of 7 days, patient had developed pneumonia,for which she was treated. History revealed that patient had global developmental delay.



Clinical examination

Development

Mental retardation, grossly delayed milestones, low pitched, weak, growling, cry in infancy.

Craniofacial

Cranium: Micro brachycephaly.

Eyes: Bushy eyebrows and synophrys, long, curly eyelashes.

Nose: Depressed nasal bridge**,** anteverted nares.

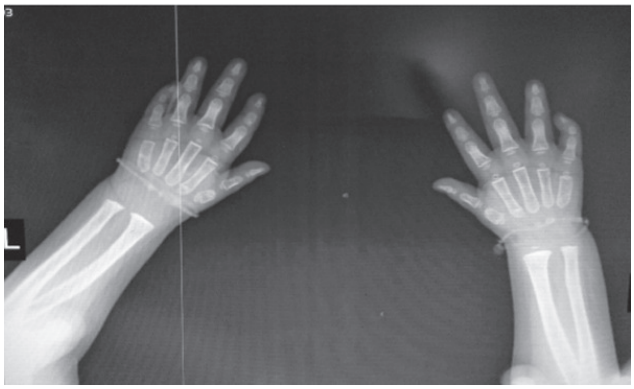
Mouth: Long philtrum, thin upper lip, and downturned angles of mouth, cleft palate,delayed eruption, crowding of teeth in maxillary arch.

Mandible: Micrognathia.

Rest of Body

Hands and arms: Micromelia, clinodactyly of fifth fingers and simian crease.

Hirsutism.



Growth Parameters

- Weight of 6kg
- Height of 73.5 cm
- Head circumference of 38 cm

S/O grade IV malnutrition, with microcephaly and short stature.

Systemic examination was normal.

Basic Blood investigations and 2D Echo was normal.

Discussion:

CdLS is a congenital anomaly syndrome characterized by distinctive facial dysmorphism, primordial short stature, hirsutism, and upper limb reduction defects, distinctcraniofacial features and low IQ ranges. Many individuals demonstrate autistic and self-destructive tendencies.[8]Currently, diagnosis is made on the basis of clinical observations. The case reported here closely confirms to the classical picture of CdLS.

The treatment of specific dental problems like erosion, gingival and periodontal disease, caries and jaw-size tooth material discrepancies should be dealt with appropriately. Also, timely referral to the medical speciality including the geneticist, cardiologist, gastroenterologist, endocrinologist, nephrologists, ophthalmologist, ENT specialist, speech therapist and occupational therapist should be met with as required.[6] Beck, discussed the postmortem examination of the patients and

revealed various congenital malformations of internal organs including cardiac defects, pulmonary hypoplasia, diaphragmatic hernias, gastrointestinal and genitourinary anomalies.[8] Van Alien demonstrated ectopic neurons in cerebral white matter in new born and microcytic changes in the kidney of some patients.[9]

Mehta DN[10] et al,reported a case of 10-year-old male patient with CdLS, who demonstrated the classic facial features of the syndrome, came with a chief complaint of decayed teeth in both upper and lower jaws. History revealed that the child had low birthweight (1.75 kg), birth asphyxia, still birth, history of convulsions at 7 months, grossly delayed milestones and also demonstrated autistic and self-destructive tendencies.

Hakan Uzun[11] et al, reported a one-day old female newborn with the complaints of seizure and multiple congenital anomalies. On examination she had arched like confluent eyebrows and well-defined, long curly eyelashes, low anterior and posterior hairline, short neck, depressed nasal bridge, down-turned angles of the mouth and thin lips, cleft palate, microcephaly, excessive body hair and small broad hands with simian creases, clinodactyly of left fifth fingers, short leg, hypertonicity, and small labia majora. On cardiac auscultation was heard 1–2/6 pansystolic murmur. Ophtalmologic examinations revealed normal findings.

In the present case, various oral and clinical features along with radiographic and other investigations were evaluated, cleft lip operation was planned with regular follow-up for any

complications and to assess overall development of the child.

Life expectancy is normal if no major malformations in Respiratory, Cardiac and Gastrointestinal system occur. Differential diagnosis includes Fryns syndrome and fetal alcohol syndrome which should be ruled out.[12] The children with CdLS usually have a wide array of health problems, making it important for all specialists to be aware of the child's special needs. Multidisciplinary treatment approach is the key to success in managing children with syndromes. The pediatric dentist may be the first health personnel to identify such a child and may lead the multidisciplinary team in treating their problems.

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